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Brief Clinical Report

Additional Case of Craniofacial and Digital Anomalies as Reported by Harrod et al.

Stanislava B. Jurenka and Margot I. Van Allen

Woodlands, B.C. Provincial Institution for the Mentally Retarded, New Westminster (S.B.J.), and Department of Medical Genetics, University of British Columbia, Vancouver (M.I.V.A.), British Columbia, Canada

In 1977 Harrod et al. [BD:OAS XIII (3B): 111–115] reported 2 brothers with an unusual syndrome of mental retardation, unusual facial appearance, large protruding ears, arachnodactyly, hypogenitalism, failure to thrive, and minor anomalies. We report on a 46-year-old man with striking resemblance to the children described by Harrod who also has secondary megacolon and varicose veins, suggesting a connective tissue disorder. © 1996 Wiley-Liss, Inc.

KEY WORDS: mental retardation, large ears, arachnodactyly, connective tissue disorder

INTRODUCTION

In 1977 Harrod et al. reported 2 brothers with a unique syndrome of unusually large and anteverted ears, thin long face, arachnodactyly, genital anomalies, mental retardation, failure to thrive, small head circumference, hypotelorism, long nose, highly arched palate, pointed chin, and a small mouth with malocclusion. An aberrant subclavian artery was found in both brothers. Both had undescended testes and hypospadias. Chromosomes were normal. The younger child also had malrotation of the small bowel and died at the age of 2 months before surgery for pyloric stenosis. Autopsy showed multiple microcysts of the renal cortex.

We report on a 47-year-old mentally retarded man with findings closely resembling those of the cases of Harrod et al. [1977]. Additional manifestations are suggestive of a connective tissue disorder.

CLINICAL REPORT

SH was born to healthy, non-consanguineous parents. He has an older normal sister whose children are adopted. Details are not available. SH was born after a pregnancy complicated by toxaemia. Birthweight was 2,520 g. The child stayed in hospital for the first 6 months of his life for unidentified respiratory problems and failure to thrive.

Psychomotor development was delayed. He walked at 4 years; presently his speech is limited to 3 single words. At about 6 years he developed constipation and generalized seizures, which responded to treatment. He was seizure free until age 41 years when he had a single brief generalized tonic clonic seizure. He had a pneumoencephalogram at the age of 7 years. Cerebral atrophy was found; the degree was not specified.

SH was admitted to a British Columbia provincial institution at the age of 14 years (Fig. 1). On admission he was tall and lean with thoracic kyphosis, a small narrow skull with strikingly large anteverted ears, large abdomen, and unusually soft hands with long hyperextensible fingers. Cardiovascular and urogenital systems were normal. His chromosomes are apparently normal and he is fragile X negative. He had a barium X-ray study, which showed a secondary megacolon.

At present, SH is ambulatory with unusual facial features, looking older than his chronological age (Figs. 2 and 3). He is 168 cm tall, weighs 68 kg, and his head circumference is 53.5 cm at the 10th centile. His face is narrow and asymmetrical. Eyes are deep set, left eye lower than the right. Hypotelorism is pronounced: intercanthal distance is 2 cm, with palpebral fissures 3.4 cm in length. The nose is quite long and deviated to the left.

Philtrum is short at 1.0 cm, and mouth is small with high arched palate. Malocclusion (forebite) with many missing teeth (removed) is noted. The chin is prominent with a small cleft. Ears are strikingly large, measuring 8 × 5.3 cm, with absence of outer folding and with a small lobule. Shoulders are narrow and he has kyphoscoliosis and mild pectus excavatum. Auscultation of heart is normal. Abdomen is large and soft. Genitalia are normal. His arm span is 181 cm as compared to a height of 168 cm. Upper to lower segment ratio is 0.846. Arachnodactyly is present, with the middle finger at the 75th centile, whereas hands are at the 50th centile.

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Address reprint requests to Margot I. Van Allen, M.D., M.Sc., Provincial Medical Genetics Programme, B.C. Children's Hospital, 4480 Oak Street, Vancouver, BC, Canada, V6H 3N1.

Fig. 1. SH at age 14.

The fingers are hyperextensible, especially in the interphalangeal joints. The larger joints also show increased laxity. Skin is hypopigmented on the back and has a velvety texture. There is some widening and tissue paper appearance to several small scars.

He has bilateral varicose veins with incipient atrophic skin changes. Deep tendon reflexes are normal. Hearing is clinically normal. Level of mental handicap was assessed as severe to profound.

Fig. 2. SH at present.

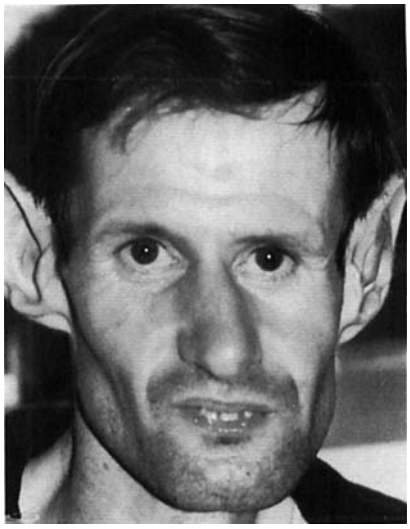

Fig. 3. SH at present.

DIAGNOSTIC STUDIES

Skeletal survey confirms both the kyphosis and a mild scoliosis. The bone density is decreased. Femoral necks are in a valgus position and the iliac wings are hypoplastic.

Barium Enema

The colon accepted between 4 and 5 L of barium. The rectosigmoid is the largest part, extending to the right hemidiaphragm. The rectum measures 13 cm across at the level of the iliac crest. No mucosal abnormality was seen.

Ophthalmologic Examination

Bilaterally immature posterior and nuclear cataracts and somewhat enlarged optic disks.

EEG in 1988

Normal record.

Blood for Atypical Homocystinuria

Negative.

Blood for HBs Ag

SH was found to be positive for hepatitis B antigen in 1986.

Echocardiogram

Normal finding.

CT Scan

Both cortical sulci and ventricles are mildly enlarged. Cavum septum pellucidum is noted. No focal changes.

DISCUSSION

Our patient has mental retardation, large ears, arachnodactyly, kyphoscoliosis, megacolon, and unusual skin, manifestations which were entered in the Oxford Dys-

TABLE I. Comparison of Patients' Characteristics in Childhood

Manifestations	Patients of Harrods et al.	Our patient
Small for gestational age	+	+
Mental retardation	+	+
Failure to thrive	+	+
Small skull	+	+
Narrow face	+	+
Hypotelorism	+	+
Pointed nose	+	+
High palate	+	+
Malocclusion	+	+
Pointed chin	+	+
Large ears	+	+
Anomaly right subclavian artery	+	−
Extropia	+	−
Arachnodactyly	+	+
Chest deformity	+	+
Hypospadias	+	−
Cryptorchidism	+	−
Renal anomalies	+	−

morphology Database. The patients reported by Harrod et al. were the only match. The findings in these patients as compared to ours are summarized in Table I. Striking similarities were also apparent when the pictures were compared.

The early life history with failure to thrive is also similar in all three. The second patient died in infancy and the autopsy did not clarify cause of death.

Our adult patient has normal cardiac findings and has no genital anomalies. Other differences: findings in our patient not identified in the original cases are the cavum septum pellucidum and the cerebral atrophy seen in the pneumoencephalogram at age 7 years and, again, on the recent CT scan, and the valgus femoral neck deformity with hypoplastic iliac wings seen on the skeletal survey. Other characteristics present in our patient are likely part of the natural history of the syndrome and include cataracts (first documented when SH was 42 years old), mild osteoporosis, kyphoscoliosis, megacolon, and varicose veins. The skin and joint characteristics are suggestive of a collagen disorder. The family was unwilling to have further studies done on our patient in order to clarify this question.

Mental retardation, asthenia, and large ears are frequent findings in a number of X-linked mental retardation syndromes. Lujan et al. in 1984 and Fryns and Buttiens in 1987 reported retarded males with marfanoid habitus; large head was identified as one of the main features of this XLMR syndrome. Both Harrod's and our patients have a small skull between 3rd and 10th centile.

Allan-Herndon-Dudley syndrome characteristics, as reviewed by Bialer et al. in 1992, include a long face, large ears, kyphosis, and severe mental retardation. Joint contractures, another feature of AHD syndrome, is not present in our patient.

Hamel et al. in 1994 reported a family with four affected males with small skull, long face, large ears, bulbous nose, and with severe heart defect. No arachnodactyly or joint laxity was present.

Several non-syndromic XLMR categories as summarized by Neri et al. in 1994 manifest large ears and hypotelorism as the only (and likely non-specific) physical anomalies.

We conclude that the similarities between our and Harrod's patients that they have a discrete MCA/MR syndrome. The question of the inheritance pattern remains unresolved. All 3 reported patients are male.

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REFERENCES

Bialer MG, Arena JF, Lawrence L, Lubs HA, Schwartz CE, Silverberg G, Stevenson RE, Williams MK (1992): Allan-Hendon-Dudley syndrome: Clinical and linkage studies on a second family. Am J Med Genet 43(1–2):491–497.

Fryns JP, Buttiens M (1987): X-linked mental retardation with marfanoid habitus. Am J Med Genet 28:267–274.

Hamel BCJ, Mariman ECM, Ropers HH, Schoonbrood-Lenssen AMJ, Van Beersum SEC (1994): Mental retardation, congenital heart defect, cleft palate, short stature, and facial anomalies. Am J Med Genet 51:591–597.

Harrod MJ, Howard J Sr, Keele DK (1977): A Syndrome of Craniofacial, Digital, and Genital Anomalies. New York: Alan R. Liss, Inc., for the National Foundation—March of Dimes. BD:OAS XIII (3B):111–115.

Lujan E, Carlin ME, Lubs HA (1984): A form of X-linked mental retardation with marfanoid habitus. Am J Med Genet 17:311–322.

Neri G, Arena JF, Chiurazzi P, Lubs HA (1994): XLMR genes: Update 1994. Am J Med Genet 51:542–549.